L Number	Hits	Search Text	DB	Time stamp
1	1	c ADJ "11" ADJ protein	USPAT	2002/12/19 14:31
2	3	c ADJ erg	USPAT	2002/12/19 14:31

09/902772

File 5:Biosis Previews(R) 1969-2002/Dec W3

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Set	Items	Description
S1	7	C()ERG
S2	4	C()11(2W)PROTEIN
S3	10	S1 OR S2
S4	79	AU='IWAMOTO MASAHIRO'
S5	10	AU='HIGUCHI YOSHINOBU'
S6	35	AU='PACIFICI MAURIZIO'
S7	7	CALIFICATION
S8	15493	CALCIFICATION
S9	4	S4 AND S8
S10	4	S4 AND S8
S11	4	S6 AND S8
S12	5	S9 OR S10 OR S11?

t s3/7/1-10

3/7/1

DIALOG(R)File 5:Biosis Previews(R)

13330612 BIOSIS NO.: 200100537761

Cell calcification supressing proteins, and genes of the proteins.

AUTHOR: Iwamoto Masahiro(a); Higuchi Yoshinobu; Pacifici Maurizio; Rosenbloom Joel

AUTHOR ADDRESS: (a)4-6-10-606, Aoshinke, Minoo-shi, Osaka 562**Japan

JOURNAL: Official Gazette of the United States Patent and Trademark Office Patents 1250 (4):pNo Pagination Sep. 25, 2001

MEDIUM: e-file

ISSN: 0098-1133

DOCUMENT TYPE: Patent

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: This invention provides cell-calcification inhibitory proteins as well as genes encoding the proteins. Based on the discovery of a novel isoform gene of the %%%c%%%-%%%erg%%% gene (herein referred to as "C-11 gene") which is an erg gene derived from chickens, the nucleotide sequence of the gene has been determined, and then the expression of a protein encoded by such gene (herein referred to as "%%%C%%%-%%%11%%% %%%protein%%%") has been confirmed. Further, it has been discovered that

when the %%%c%%%-%%%erg%%% or C-11 gene is introduced into osteoblasts, the calcification of the cells is inhibited.

3/7/2
DIALOG(R)File 5:Biosis Previews(R)

13112411 BIOSIS NO.: 200100319560
Complementary effects of Mediterranean diet and moderate red wine intake on haemostatic cardiovascular risk factors.
AUTHOR: Mezzano D(a); Leighton F; Martinez C; Marshall G; Cuevas A; Castillo O; Panes O; Munoz B; Perez D D; Mizon C; Rozowski J; San Martin A; Pereira J
AUTHOR ADDRESS: (a)Haemostasis Laboratory, Department of Hematology-Oncology, School of Medicine, Catholic University, Santiago: dmezzano@med.puc.cl**Chile
JOURNAL: European Journal of Clinical Nutrition 55 (6):p444-451 June, 2001
MEDIUM: print
ISSN: 0954-3007
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Objectives: To compare the effect of alcohol-free Mediterranean-type diet (MD) and high-fat diet (HFD) on plasma concentration of emergent haemostatic cardiovascular risk factors (HCVRF). Also, to test if red wine supplementation modifies HCVRF, independent of diet. Design, subjects and intervention: Controlled prospective intervention study. Two groups, each of 21 healthy male university students (22+3.4 y), received either MD or HFD for 90 days. Between days 30 and 60, both diets were supplemented with 240 ml/day of red wine. Baseline and T30, T60 and T90-day samples were drawn. No drop out from the study was observed. Setting: University campus and outpatient nutrition clinic. Results: Volunteers on HFD at T30 had increases in pro-coagulants fibrinogen (22%), factor VIIc (9%), and factor VIIIc (4%), and decreases in natural anticoagulants antithrombin III (3%), protein %%%C%%% (%%%11%%%%) and %%%protein%%% S (6%) and of 20% in plasminogen activator inhibitor-1. At the same time, individuals on MD had increases in fibrinogen (4%), antithrombin III (5%), protein C (3%), protein S (2.7%), and decreases in factor VIIIc (9%), and plasminogen activator inhibitor-1 (21%). After adjusting by baseline values, MD was associated with lower plasma fibrinogen (P=0.03), factor VIIc (P=0.034) and factor VIIIc (P=0.0057) and with higher levels of protein S (P=0.013). Red wine supplementation, in both diets, resulted in decreased

plasma fibrinogen (P=0.001) and factor VIIc (P=0.05), and increased tissue plasminogen activator antigen (P=0.01) and plasminogen activator inhibitor-1 antigen (P=0.0003). Wine consumption was also associated with significantly (P=0.01) divergent effects on antithrombin III: it decreased by 10% in individuals on HFD but increased slightly in those on MD. No effects of diet or wine were detected in plasma protein C and C-reactive protein. Conclusion: MD and moderate consumption of red wine have complementary, mostly beneficial effects on HCVRF.

8/7/3
DIALOG(R)File 5:Biosis Previews(R)

11124552 BIOSIS NO.: 199799745697
Serotonin elevates the c-wave of the electroretinogram of the rabbit eye by increasing the transepithelial potential.
AUTHOR: Bragadottir Ragnheidur(a); Kato Masaru; Jarkman Sven
AUTHOR ADDRESS: (a)Dep. Ophthalmol., Linkoping Univ., S-581 85 Linkoping** Sweden
JOURNAL: Vision Research 37 (18):p2495-2503 1997
ISSN: 0042-6989
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The influence of serotonin (5-hydroxytryptamine, 5-HT) and serotonin analogues on the direct current electroretinogram (d.%%%c%%%. %%%ERG%%%) and the standing potential of the albino rabbit eye (SP) was studied. After unilateral vitrectomy, corneal recordings were obtained during simultaneous intravitreal perfusion with a control solution alternating with 5-HT at concentrations of 25, 120 and 200 mu-M. The c-wave increased at 25 and 120 mu-M when changing from control solution to test solution (P lt 0.05) but did not decrease significantly when changing back to control solution (P gt 0.05). The c-wave was reversibly elevated at 200 mu-M (PHS-5-HT, P lt 0.01; 5-HT-PHS, P lt 0.05). To analyse further the influence on the c-wave, in vivo intraretinal microelectrode recordings were obtained during intravitreal perfusion with 5-HT. The transepithelial potential (TEP) increased (P lt 0.01), while the slow PIII was not significantly affected (P gt 0.05). The serotonin receptor agonists 1-(2,5-dimethoxy-4-iodophenyl)-2-aminopropane, 5-methoxytryptamine, alpha-methyl-5-hydroxytryptamine and 2-methyl-5-hydroxytryptamine, caused a significant reversible elevation of the c-wave, whereas 5-carboxyamidotryptamine did not. Tropisetron did not block the serotonin effect and LY53857 had an effect of its own on the c-wave. The results seem to indicate that the influence of serotonin on the c-wave is mainly

due to an effect on the retinal pigment epithelium (RPE) and that more than one type of serotonin receptor may be involved.

3/7/4
DIALOG(R)File 5:Biosis Previews(R)

10697574 BIOSIS NO.: 199799318719
A cAMP response element and an Ets motif are involved in the transcriptional regulation of flt-1 tyrosine kinase (vascular endothelial growth factor receptor 1) gene.
AUTHOR: Wakiya Kenji; Begue Agnes; Stehelin Dominique; Shibuya Masabumi(a)
AUTHOR ADDRESS: (a)Dep. Genet., Inst. Medical Sci., Univ. Tokyo, Minato-ku, Tokyo 108**Japan
JOURNAL: Journal of Biological Chemistry 271 (48):p30823-30828 1996
ISSN: 0021-9258
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The flt-1 gene encodes a transmembrane tyrosine kinase, Flt-1, a receptor for vascular endothelial growth factor. The expression of flt-1 gene is restricted to endothelial cells in vivo. To understand the molecular mechanism underlying endothelial-specific expression of this gene, we studied the functional significance of transcriptional motifs in the 200-base pair region of the human flt-1 gene promoter, which has been identified to confer cell type specificity. By point mutation analysis using chloramphenicol acetyltransferase plasmids in 293E1 cells, which express significant levels of flt-1 mRNA, we found that an Ets motif, E4, at -54 to -51 and a cAMP response element (CRE) at -83 to -76 are involved in the transcriptional regulation of this gene. Disruption of either this CRE or E4 within the promoter sequence of 90 base pairs resulted in a decrease in chloramphenicol acetyltransferase activity of 90%, indicating that co-existence of both of CRE and Ets motif E4 is necessary for transcription of the flt-1 gene. Co-transfection of an expression vector containing c-ets- 1, c-ets-2, or %%%c%%%-%%%erg%%% cDNA with this 90-base pair sequence yielded a 5-8-fold elevation of chloramphenicol acetyltransferase activity, further supporting the idea that Ets family protein(s) participates in the regulation of the flt-1 gene. Gel shift assays using nuclear extracts of 293E1 and endothelial cells demonstrated the existence of protein factor(s) that specifically binds to CRE and Ets motif E4, respectively. Taken together, our results strongly suggest cooperation of a CRE and an Ets motif for the function of the flt-1 gene promoter.

3/7/5

DIALOG(R)File 5:Biosis Previews(R)

10302892 BIOSIS NO.: 199698757810

Kainic acid effects on neural retina and retinal pigment epithelium-A.D. %%%C%%%. %%%ERG%%% study of the albino rabbit eye.

AUTHOR: Bragadottir R; Nilsson S E G; Jarkman S H

AUTHOR ADDRESS: Dep. Ophthalmol., Linkoping Univ., Linkoping**Sweden

JOURNAL: Investigative Ophthalmology & Visual Science 37 (3):pS349 1996

CONFERENCE/MEETING: 1996 Annual Meeting of the Association for Research in Vision and Ophthalmology Fort Lauderdale, Florida, USA April 21-26, 1996

ISSN: 0146-0404

RECORD TYPE: Citation

LANGUAGE: English

3/7/6

DIALOG(R)File 5:Biosis Previews(R)

09894258 BIOSIS NO.: 199598349176

PET tracers for assessing liver metabolism: (1-%%%C%%%-%%%11%%%)tyrosine for %%%protein%%% synthesis and (methyl-C-11)methionine for phospholipid synthesis.

AUTHOR: Ishiwata K(a); Enomoto K; Sasaki T(a); Elsinga P H; Senda M(a); Okazumi S; Isono K; Paans A M J; Vaalburg W

AUTHOR ADDRESS: (a)Positron Med. Cent., Tokyo Metropolitan Inst. Gerontol., Tokyo**Japan

JOURNAL: Journal of Nuclear Medicine 36 (5 SUPPL.):p152P 1995

CONFERENCE/MEETING: 42nd Annual Meeting of the Society of Nuclear Medicine Minneapolis, Minnesota, USA June 12-15, 1995

ISSN: 0161-5505

RECORD TYPE: Citation

LANGUAGE: English

3/7/7

DIALOG(R)File 5:Biosis Previews(R)

09812122 BIOSIS NO.: 199598267040

Human ERG is a proto-oncogene with mitogenic and transforming activity.

AUTHOR: Hart Adam H; Corrick Catherine M; Tymms Martin J; Hertzog Paul J; Kola Ismail(a)

AUTHOR ADDRESS: (a)Molecular Embryol. Birth Defects Lab., Inst.

Reproduction Dev., Monash Univ, Monash Med. Centre,**Australia
JOURNAL: Oncogene 10 (7):p1423-1430 1995
ISSN: 0950-9232
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The ETS related gene, ERG, is one of 20 or more genes belonging to the ETS family of transcription factors. Translocation of the ERG gene t(21;22) results in the chimeric fusion transcript seen in approximately 10% of Ewings sarcomas. In addition, recent studies have shown that a reciprocal translocation t(21;16) of ERG gives rise to two aberrant transcripts seen in some forms of acute myeloid leukaemia. In vitro studies have linked the up regulation of ERG expression with stromal cell independence in erythroleukemic clones and shown that the ERG related genes ETS1 and ETS2 have a mitogenic and transforming activity when overexpressed in NIH3T3 cells. Interestingly ERGB/FLI-1, which is also involved in Ewings sarcoma translocations and shares a very high sequence identity with ERG has been reported to be unable to transform NIH3T3 cells. In this study we investigate the effects of overexpression of ERG on cell proliferation, factor dependence, growth in soft agar and tumorigenesis in nude mice. An ERG expression construct with the human ERG2 cDNA driven by the sheep metallothionein Ia promoter (sMTERG) was transfected into NIH3T3 cells. Clonal cell lines overexpressing ERG were established. The cell lines became morphologically altered, grew in low serum and serum free media and gave rise to colonies in soft agar suspension. Furthermore, we demonstrate that after subcutaneous injection these clones grow as solid tumors in nude mice. These data demonstrate that %%%c%%%-%%%ERG%%% is a proto-oncogene capable of transforming NIH3T3 cells. Therefore, overexpression or inappropriate expression of ERG may contribute to oncogenesis.

3/7/8

06621150 BIOSIS NO.: 000087063312
THE DC-RECORDED DOG ELECTRORETINOGRAM IN KETAMINE-MEDETOMIDINE ANESTHESIA
AUTHOR: KOMMONEN B
AUTHOR ADDRESS: DEP. SURGERY, COLL. VET. MED., HAMEENTIE 57, SF-00550 HELSINKI, FINLAND.
JOURNAL: ACTA VET SCAND 29 (1). 1988. 35-42. 1988
FULL JOURNAL NAME: Acta Veterinaria Scandinavica
CODEN: AVSCA
RECORD TYPE: Abstract

LANGUAGE: ENGLISH

ABSTRACT: A new selective alpha 2-adrenoreceptor agonist, medetomidine hydrochloride, was combined with low dosage ketamine hydrochloride and vecuronium bromide for d.c. (direct current) recordings of fast electroretinographic (ERG) components in nine ophthalmoscopically healthy dark adapted dogs. The dogs were tracheally intubated and manually ventilated. They were given full field single flash stimuli of different intensities starting with near b-wave threshold blue light (tests 1-3), followed by white light (tests 4-6) and 30 Hz photopic flicker (test 7). The a- and b-wave amplitudes and flicker responses were measured from the base line. The latencies were measured from the stimulus moment to the highest point of the different waves. Statistical analysis of results gave individual differences which had a good constancy. This showed that the dogs had an individual ERG profile according to the standardized method. The latencies varied very little as expected, but the amplitude differed individually and showed a good constancy as seen by reproducibility tests made nine to ten days later on three of the dogs' ipsilateral eyes. The combination of drugs used in this study was considered suitable for short term (10-12 minutes) stable d.%%%c%%%.-%%%ERG%%% recordings in dogs as the rod and cone responses had higher amplitudes when compared to an identical examination made with other anaesthetic combinations on the same dogs. Involuntary eye movements and other involuntary muscular activity caused by ketamine in dogs were negligible when using medetomidine premedication and was completely absent when using vecuronium. The anaesthetic method described can be recommended for ambulatory ERG recordings in dogs because of the above mentioned advantages.

3/7/9

05607854 BIOSIS NO.: 000083080994

MECHANISMS OF AZIDE INDUCED INCREASES IN THE C-WAVE AND STANDING POTENTIAL OF THE INTACT CAT EYE

AUTHOR: LINSENMEIER R A; STEINBERG R H

AUTHOR ADDRESS: DEPARTMENT OF PHYSIOLOGY AND OPHTHALMOLOGY, UNIVERSITY OF CALIFORNIA, SAN FRANCISCO, CALIF. 94143, USA.

JOURNAL: VISION RES 27 (1). 1987. 1-8. 1987

FULL JOURNAL NAME: Vision Research

CODEN: VISRA

RECORD TYPE: Abstract

LANGUAGE: ENGLISH

ABSTRACT: The c-wave of the ERG and the standing potential of the eye both undergo increases in amplitude following intravenous infusion of sodium azide (NaN3), as first shown by Noell [Am. J. Physiol, 170, 217-238 (1952); U.S.A.F. School of Aviation Medicine, Project No. 21-1201-004 (1953)]. We have studied the mechanism of these changes in the intact eye. Intraretinal and intracellular retinal pigment epithelial (RPE) cell recordings showed that most of the change occurs at the RPE, but that there is a small direct effect on the neural retina. The increase of standing potential is caused by a depolarization of the basal membrane of the RPE, and the increase in c-wave amplitude results from a decrease in basal membrane resistance that accompanies the depolarization. This relation between basal membrane potential and resistance is similar to that observed during hypoxia and during the light peak of the d.%%%c%%%. %%%ERG%%%.

3/7/10
DIALOG(R)File 5:Biosis Previews(R)

03910038 BIOSIS NO.: 000075088111
IDENTIFICATION AND CHARACTERIZATION OF AN IMMUNOLOGICALLY CONSERVED ADENOVIRUS EARLY REGION 11000 MOLECULAR WEIGHT PROTEIN AND ITS ASSOCIATION WITH THE NUCLEAR MATRIX
AUTHOR: SARNOW P; HEARING P; ANDERSON C W; REICH N; LEVINE A J
AUTHOR ADDRESS: STATE UNIV. NEW YORK STONY BROOK, DEP. MICROBIOL., SCH. MED. STONY BROOK, N.Y. 11794, USA.
JOURNAL: J MOL BIOL 162 (3). 1982. 565-584. 1982
FULL JOURNAL NAME: Journal of Molecular Biology
CODEN: JMOBA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Antisera from some hamsters bearing adenovirus-induced tumors contain antibodies to an 11,000 MW adenovirus-induced protein. In adenovirus-infected human cervical carcinoma HeLa cells, this early viral protein was specifically associated with the nuclear matrix fraction. After 2-dimensional gel electrophoresis, 2 forms of the 11,000 MW protein at pI [isoelectric point] 5.6 and 5.4 were found. Only the pI 5.4 form of this protein was associated with the nuclear matrix fraction. Adenoviruses from groups A, B, C, D and E all produced an early viral protein (10,000-12,000 MW) that reacted with group C antibody to the 11,000 MW protein. To date, this is the only known early viral protein that is immunologically conserved in all of the human adenovirus groups. The positions of 2 methionine and 7 leucine residues were determined by sequencing the first 35 amino acids from the N terminus of the adenovirus

serotype 2 group %%%C%%% %%%11%%%,000 MW %%%protein%%%. The positions of these amino acid residues were compared to the adenovirus serotype 2 nucleotide sequence, which uniquely localized the structural gene of the 11,000 MW protein to region E4, subregion 3 in type 2 adenovirus. A frameshift mutant, which contained a deletion of 1 base-pair in the structural gene of the 11,000 MW protein, was isolated and mapped by marker rescue and nucleotide sequence analysis. This mutant had a viable phenotype, producing normal levels of infectious virus in both HeLa cells and human embryo lung WI38 cells in culture. These experiments identify the first adenovirus early region 4 protein detected in virus-infected cells.

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12/7/1

DIALOG(R)File ..5:Biosis Previews(R)

13973847 BIOSIS NO.: 200200602668

The Wnt antagonist Frzb-1 regulates chondrocyte maturation and long bone development during limb skeletogenesis.

AUTHOR: Enomoto-Iwamoto Motomi(a); Kitagaki Jirouta; Koyama Eiki; Tamamura Yoshihiro; Wu Changshan; Kanatani Naoko; Koike Tatsuya; Okada Hiroshi; Komori Toshihisa; Yoneda Toshiyuki; Church Vicki; Francis-West Philippa H ; Kurisu Kojiro; Nohno Tsutomu; %%%Pacifici Maurizio%%%; %%%Iwamoto%%% %%% Masahiro%%%

AUTHOR ADDRESS: (a)Departments of Molecular, Cell and Tumor Biology, Faculty of Dentistry, Osaka University, Suita, Osaka, 565-0871**Japan E-Mail: motomi@dent.osaka-u.ac.jp, Motomi.Iwamoto@mail.tju.edu

JOURNAL: Developmental Biology 251 (1):p142-156 November 1, 2002

MEDIUM: print

ISSN: 0012-1606

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: The Wnt antagonist Frzb-1 is expressed during limb skeletogenesis, but its roles in this complex multistep process are not fully understood. To address this issue, we determined Frzb-1 gene expression patterns during chick long bone development and carried out gain- and loss-of-function studies by misexpression of Frzb-1, Wnt-8 (a known Frzb-1 target), or different forms of the intracellular Wnt mediator LEF-1 in developing limbs and cultured chondrocytes. Frzb-1 expression was quite strong in mesenchymal prechondrogenic condensations and then characterized epiphyseal articular chondrocytes and prehypertrophic chondrocytes in growth plates. Virally driven Frzb-1 misexpression caused shortening of skeletal elements, joint fusion, and

delayed chondrocyte maturation, with consequent inhibition of matrix mineralization, metalloprotease expression, and marrow/bone formation. In good agreement, misexpression of Frzb-1 or a dominant-negative form of LEF-1 in cultured chondrocytes maintained the cells at an immature stage. Instead, misexpression of Wnt-8 or a constitutively active LEF-1 strongly promoted chondrocyte maturation, hypertrophy, and %%%calcification%%%. Immunostaining revealed that the distribution of endogenous Wnt mediator beta-catenin changes dramatically in vivo and in vitro, from largely cytoplasmic in immature proliferating and prehypertrophic chondrocytes to nuclear in hypertrophic mineralizing chondrocytes. Misexpression of Frzb-1 prevented beta-catenin nuclear relocalization in chondrocytes in vivo or in vitro. The data demonstrate that Frzb-1 exerts a strong influence on limb skeletogenesis and is a powerful and direct modulator of chondrocyte maturation, phenotype, and function. Phases of skeletogenesis, such as terminal chondrocyte maturation and joint formation, appear to be particularly dependent on Wnt signaling and thus very sensitive to Frzb-1 antagonistic action.

12/7/2
DIALOG(R)File 5:Biosis Previews(R)

13330612 BIOSIS NO.: 200100537761
Cell %%%calcification%%% supressing proteins, and genes of the proteins.
AUTHOR: %%%Iwamoto Masahiro%%%(a); Higuchi Yoshinobu; %%%Pacifici%%% %%% Maurizio%%%; Rosenbloom Joel
AUTHOR ADDRESS: (a)4-6-10-606, Aoshinke, Minoo-shi, Osaka 562**Japan
JOURNAL: Official Gazette of the United States Patent and Trademark Office Patents 1250 (4):pNo Pagination Sep. 25, 2001
MEDIUM: e-file
ISSN: 0098-1133
DOCUMENT TYPE: Patent
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: This invention provides cell-%%%calcification%%% inhibitory proteins as well as genes encoding the proteins. Based on the discovery of a novel isoform gene of the c-erg gene (herein referred to as "C-11 gene") which is an erg gene derived from chickens, the nucleotide sequence of the gene has been determined, and then the expression of a protein encoded by such gene (herein referred to as "C-11 protein") has been confirmed. Further, it has been discovered that when the c-erg or C-11 gene is introduced into osteoblasts, the %%%calcification%%% of the cells is inhibited.

12/7/3
DIALOG(R)File 5:Biosis Previews(R)

10985888 BIOSIS NO.: 199799607033
Regulation production of mineralization-competent matrix vesicles in hypertrophic chondrocytes.
AUTHOR: Kirsch Thorsten(a); Nah Hyun-Duck; Shapiro Irving M; %%%Pacifici%%% %%% Maurizio%%%(a
AUTHOR ADDRESS: (a)Dep. Anatomy Histology, Sch. Dental Med., Univ. Pennsylvania, 4001 Spruce St., Philadelphia, PA **USA
JOURNAL: Journal of Cell Biology 137 (5):p1149-1160 1997
ISSN: 0021-9525
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Matrix vesicles have a critical role in the initiation of mineral deposition in skeletal tissues, but the ways in which they exert this key function remain poorly understood. This issue is made even more intriguing by the fact that matrix vesicles are also present in nonmineralizing tissues. Thus, we tested the novel hypothesis that matrix vesicles produced and released by mineralizing cells are structurally and functionally different from those released by nonmineralizing cells. To test this hypothesis, we made use of cultures of chick embryonic hypertrophic chondrocytes in which mineralization was triggered by treatment with vitamin C and phosphate. Ultrastructural analysis revealed that both control nonmineralizing and vitamin C/phosphate-treated mineralizing chondrocytes produced and released matrix vesicles that exhibited similar round shape, smooth contour, and average size. However, unlike control vesicles, those produced by mineralizing chondrocytes had very strong alkaline phosphatase activity and contained annexin V, a membrane-associated protein known to mediate Cal' influx into matrix vesicles. Strikingly, these vesicles also formed numerous apatite-like crystals upon incubation with synthetic cartilage lymph, while control vesicles failed to do so. Northern blot and immunohistochemical analyses showed that the production and release of annexin V-rich matrix vesicles by mineralizing chondrocytes were accompanied by a marked increase in annexin V expression and, interestingly, were followed by increased expression of type I collagen. Studies on embryonic cartilages demonstrated a similar sequence of phenotypic changes during the mineralization process in vivo. Thus, chondrocytes located in the hypertrophic zone of chick embryo tibial growth plate were characterized by strong annexin V expression, and those located at the chondro-osseous mineralizing border exhibited expression of both annexin V and type I collagen. These findings reveal that hypertrophic chondrocytes can

qualitatively modulate their production of matrix vesicles and only when induced to initiate mineralization, will release mineralization-competent matrix vesicles rich in annexin V and alkaline phosphatase. The occurrence of type I collagen in concert with cartilage matrix %%%calcification%%% suggests that the protein may facilitate crystal growth after rupture of the matrix vesicle membrane; it may also offer a smooth transition from mineralized type II/type X collagen-rich cartilage matrix to type I collagen-rich bone matrix.

12/7/4

09017558 BIOSIS NO.: 199497025928

Effects of interleukin-1 on syntheses of alkaline phosphatase, type X collagen, and 1,25-dihydroxyvitamin D-3 receptor, and matrix %%%calcification%%% in rabbit chondrocyte cultures.

AUTHOR: Kato Yukio(a); Nakashima Kazuhisa; %%%Iwamoto Masahiro%%%; Murakami Hiroshi; Hiranuma Hiroko; Koike Tatsuya; Suzuki Fujio; Fuchihata Hajime; Ikehara Yukio; Noshiro Mitsuhide; Jikko Akitoshi
AUTHOR ADDRESS: (a)Dep. Biochem., Sch. Dent., Hiroshima Univ., 1-2-3 Kasumi, Minami-ku, Hiroshima 734**Japan

JOURNAL: Journal of Clinical Investigation 92 (5):p2323-2330 1993
ISSN: 0021-9738
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The effect of IL-1 on expression of the mineralization-related phenotype by chondrocytes was examined. In cultures of rabbit growth plate chondrocytes, IL-1 beta at 0.1 ng/ ml caused 95% decreases in alkaline phosphatase activity, alkaline phosphatase mRNA levels, the incorporation of 45Ca into insoluble material, and the calcium content during the hypertrophic stage. These effects of IL-1 beta were dose-dependent and were observed in 24-48 h. Furthermore, IL-1 beta suppressed increase in cell size and the syntheses of 1,25-dihydroxyvitamin D-3 receptor and type X collagen, other markers of hypertrophy, but had little effect on the synthesis of total protein including type II collagen. The inhibition of %%%calcification%%% was observed only when chondrocytes were exposed to IL-1 before the onset of %%%calcification%%%: IL-1 treatment from the mineralization stage had a marginal effect on 45Ca incorporation into insoluble material. These results suggest that IL-1 inhibits chondrocyte hypertrophy and the onset of %%%calcification%%% in ossifying cartilage.

12/7/5

DIALOG(R)File 5:Biosis Previews(R)

08932401 BIOSIS NO.: 199396083902

Retinoic acid induced rapid mineralization and expression of mineralization-related genes in chondrocytes.

AUTHOR: %%%Iwamoto Masahiro%%%(a); Shapiro Irving M; Yagami Kimitoshi(a); Boskey Adele L; Leboy Phoebe S; Adams Sherrill L; %%%Pacifici Maurizio%%% (a

AUTHOR ADDRESS: (a)Skeletal Biol. Research Group, Dep. Anatomy-Histol., Sch. Dental Med., Univ. Pennsylvania, Phila**USA

JOURNAL: Experimental Cell Research 207 (2):p413-420 1993

ISSN: 0014-4827

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: Numerous studies of experimental hypo- and hypervitaminosis A have long suggested that retinoic acid (RA) is involved in chondrocyte maturation during endochondral ossification and skeletogenesis. However, the specific and direct roles of RA in these complex processes remain unclear. Based on recent studies from our laboratories, we tested the hypothesis that RA induces the expression of genes associated with the terminal mineralization phase of chondrocyte maturation and promotes apatite deposition in the extracellular matrix. Cell populations containing chondrocytes at advanced stages of maturation were isolated from the upper portion of Day 18 chick embryo sterna and grown for 2 weeks in monolayer until confluent. The cells were then treated with low doses (10-100 nM) of RA for up to 6 days in the presence of a phosphate donor (beta-glycerophosphate) but in the absence of ascorbic acid. Within 4 days of treatment, RA dramatically induced expression of the alkaline phosphatase (APase), osteonectin, and osteopontin genes, caused a several-fold increase in APase activity, and provoked massive mineral formation while it left type X collagen gene expression largely unchanged. The mineral had a mean Ca/P-i molar ratio of 1.5; Fourier transform infrared spectra confirmed that it represented hydroxyapatite. Mineralization was completely abolished by treatment with parathyroid hormone; this profound effect confirmed that RA induced cell-mediated mineralization and not nonspecific precipitation. When cultures were treated with both RA and ascorbic acid, there was a slight further increase in APase activity and increased calcium accumulation. The effects of RA were also studied in cultures of immature chondrocytes isolated from the caudal portion of sternum; however, RA only had minimal effects on mineralization and gene expression in these cells. Thus, RA

appears to be a rapid, potent, maturation-dependent,
ascorbate-independent promoter of terminal maturation and matrix
%%%calcification%%% in chondrocytes.

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$39.69 Estimated cost this search
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